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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/270,910	03/16/1999	HANS HENRIK IPSEN	4305/1E144-U	3210

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	27

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/270,910	Applicant(s) IPSEN ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-14,16-34 and 40-51* is/are pending in the application.

4a) Of the above claim(s) *29-31 and 40-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-14,16-34,40-49 and 51* is/are rejected.

7)☒ Claim(s) *50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/10/02 has been entered.

2. Claims 2-14, 16-34 and 40-51 are pending.

3. Claims 29-31 and 40-46 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to a non-elected inventions.

4. Applicant is advised that should claim 4 be found allowable, claim 49 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

5. Claim 50 is objected to because "an" as recited in line 2 should have been deleted.

6. Claim 28 is objected to under 37 CFR 1.821(d) because SEQ ID NO is required. Appropriate correction is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 2-14, 16-28, 32-34, 47-49 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a recombinant mutant allergen from birch pollen major allergen of SEQ ID NO: 37 having one or more amino acid substitutions such as the ones disclosed on page 27 lines 25-32 or the ones recited in claim 50 and (2) a recombinant

mutant allergen from Ves v 5 of SEQ ID NO: 38-39 having one or more amino acid substitutions such as the ones disclosed on page 44-46 obtainable by the method recited in claim 2 for treating allergic reactions, **does not** reasonably provide enablement for (1) *any* recombinant mutant allergen derived from *any* naturally occurring allergen in which at least one surface-exposed, *any* amino acid residue of a B cell epitope at *any* position which is conserved in *any* amino acid sequences of *any* homologous proteins within the taxonomic order from which the naturally occurring allergen originates, is substituted with *any* amino acid residue which is not conserved in the same position in the amino acid sequences of any homologous proteins within the taxonomic order from which the naturally occurring allergen originates, wherein the α-carbon backbone tertiary structure of *any* naturally occurring allergen, and specific IgE binding to *any* mutant allergen is reduced compared to the IgE binding to *any* naturally occurring allergen, (2) *any* recombinant allergen mentioned above obtainable by a) identifying *any* amino acid residues in *any* naturally occurring allergen which are conserved with more than 70% identity in all known homologous proteins within the taxonomic order from which said naturally occurring allergen originates, (b) defining at least one patch of conserved amino acid residues being coherently connected over at least 400 $Å^2$ of the surface of the thee-dimensional structure of *any* naturally occupying allergen molecule as defined by having a solvent accessibility of at least 20%, said at least one patch comprising at least one B cell epitope and (c) substituting at least *any* one amino acid residue in said *any* one patch with another non-conservative amino acid, wherein the α-carbon backbone tertiary structure of the allergen molecule is conserved, (3) *any* recombinant allergen mentioned above wherein the specific IgE binding to the mutant allergen is reduced by at least 5%, preferably by at least 10%, (4) *any* recombinant allergen mentioned above wherein the average root mean square deviation of the atomic coordinates comparing the α-carbon backbone tertiary structures of *any* mutant and the naturally occurring allergen molecules is below 2 Å, (5) *any* recombinant allergen obtainable by the process of claim 2 wherein said at least *any* one patch consisting of *any* 15 amino acid residues, (6) *any* recombinant allergen obtainable by the process of claim 2 wherein the amino acid residues of *any* one patch are ranked with respect to solvent accessibility and *any* one or more amino acids among the more solvent accessible ones are substituted, (7) *any* recombinant allergen mentioned above wherein one or more amino acid residues of *any* one patch having a solvent accessibility of 20-80% are substituted, *any* 1-5 amino acids residues per 400 $Å^2$ in any one patch are substituted, *any* substitution of one or more amino acid residues in any B cell epitope or *any* one patch is carried out by site-directed mutagenesis,

(8) *any* recombinant allergen mentioned above wherein the allergen is derived from *any* inhalation allergen, *any* pollen allergen, *any* pollen allergen originating from the taxonomic order of Fagales, Oleales or inales, (9) *any* recombinant allergen derived from Bet v1 wherein at least *any* one amino acid residues of said B cell epitope or said at least *any* one patch is substituted, (10) *any* recombinant allergen mentioned above derived from inhalation allergen wherein the allergen is a pollen allergen derived from *any* pollen allergen originating from the taxonomic order of Poales, Asterales, or Urticales, house dust mite, mite allergen from Dermatophagoides, cockroach allergen, *any* animal allergen such as the ones from cat, dog or horse, venom allergen originating from the taxonomic order of Hymenoptera, Vespidae, Apidae and Formicoidae, *any* allergen derived from Ves v5 (11) *any* recombinant allergen wherein the allergen is derived from any venom allergen wherein at least one amino acid is substituted such as the substitution is from Lys to Ala at position 72 or from Tyr to Ala at position 96, (12) *any* recombinant allergen mentioned above for use as a pharmaceutical, (13) *any* pharmaceutical composition comprising *any* recombinant allergen mentioned above optionally in combination with *any* pharmaceutical acceptable carrier and/or excipient, and optionally an adjuvant, (14) *any* pharmaceutical composition mentioned above in the form of a vaccine against allergic reactions elicited by any naturally occurring allergen in patients suffering from allergy, (15) *any* pharmaceutical composition obtainable by the process such as the process recited in claim 48, and (16) *any* recombinant allergen obtainable by the process recited in claim 2 wherein said at least one patch consists of at least *any* 15 amino acid residues, or *any* 15-25 amino acid residues for a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only two recombinant allergens from birch pollen major allergen comprising SEQ ID NO: 37 from the taxonomic order of *Fagales* and vaspid venom Ves v 5 comprising SEQ ID NO: 38-39 from the taxonomic order of Hymenoptera. The specification discloses recombinant mutant allergen from birch pollen major allergen comprising SEQ ID NO: 37 wherein said allergen has one or more amino acid substitutions such as the ones disclosed on page 27 lines 25-32 of the specification or the ones recited in claim 50. The specification further discloses recombinant mutant allergen from vaspid venom Ves v 5 comprising SEQ ID NO: 38-39 having one or more amino acid substitutions such as the ones disclosed on page 44-46. The said recombinant mutant allergens obtainable by the method recited in claim 2 for treating allergic reactions.

Other than the specific amino acid substitutions in the specific allergens of SEQ ID NO: 37-39 mentioned above, the specification does not teach how to make and use *any* recombinant mutant allergen such as inhalation allergen from the taxonomic order of *Oleales*, *Pinales*, *Asterales*, *Urticales*, allergen from a house dust mite originating from *Dermatophagoides*, cockroach allergen, or animal allergen originating from a cat, dog or horse in which at least one surface-exposed amino acid residues of any B cell epitope at any position which is conserved in the amino acid sequences of homologous proteins within the taxonomic order from which the naturally occurring allergen originates is substituted with *any* amino acid residue which is not conserved in the same position wherein the recombinant mutant allergen has an α-carbon backbone tertiary structure essentially the same as the α-carbon backbone tertiary structure of the naturally occurring allergen and specific IgE binding to the mutant allergen is reduced compared to the IgE binding to the naturally occurring allergen wherein the specific IgE binding to the mutant is reduced by at least 5%, preferably at least 10% wherein at least one patch of conserved amino acid residues comprises atoms of 15-25 amino acid residues ranked with respect to solvent accessibility and one ore more amino acids among the more solvent accessible ones are substituted for a pharmaceutical composition or a vaccine.

There is insufficient guidance and working example as to which amino acid residues within the B cell epitope such as any patch of amino acid residues consisting of at least 15 amino acids or 15-25 amino acid residues in length of any inhale allergen from any taxonomic order such as *Oleales*, *Pinales*, *Asterales*, *Urticales*, allergen from a house dust mite originating from *Dermatophagoides*, cockroach allergen, or animal allergen originating from a cat, dog or horse that can be substitute and whether after amino acid substitutions would maintain the α-carbon

backbone tertiary structure and reduced IgE binding at least 5%, or at least 10% as compared to the naturally occurring allergen, in turn, would be useful for a pharmaceutical composition or a vaccine against any allergen. It is well known in the art that the relationship between the sequence of a protein and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495).

The state of the prior art as exemplified by Lebecque *et al*, Gajhede *et al* and Elsayed *et al* (all of record) is such that determining the IgE binding of Bet v 1 (B cell epitope) is conformational dependent by nature, including applicants' disclosure on page 36 bridging to page 37. Given the diversity of B cell epitope ranging from conformational to linear epitope structures, there is no predictability regarding what effect amino acid substitutions will have on the structure and function of all allergen to which the antibody binds because it is difficult to predict the 3-D structure of modified allergens from a primary structure such as amino acid sequence alignment, in turn, would be useful for a vaccine against all allergy. The predictability of making modified allergens mentioned above is limited to factors such as the mutagenesis method. Given the insufficient guidance and working examples, predicting what changes can be made to the amino acid sequence of any allergen mentioned above that after substitution, will retain both structure and reduce IgE function *in vivo* is unpredictable. Since the specification fails to provide guidance regarding which amino acid can tolerate change, it follows that any allergen mentioned above other than Bet v I from the taxonomic order of *Fagales* and vaspid venom Ves v 5 from the taxonomic order of Hymenoptera is not enable.

With regard to a pharmaceutical composition and vaccine comprising any recombinant mutant allergen, there are no in vivo working example demonstrating any recombinant mutant allergen mentioned above is effective in prevent any allergy. There are no showing of any recombinant mutant allergen mentioned above, other than Bet v 1 and Ves v 5, that reduce IgE binding for the specific allergies. Even if IgE binding is reduced by 5% or by 10%, there is still a 95% or 90% chance that the mutant allergen could bind IgE and induce anaphylaxis. A vaccine in the absence of in vivo data is unpredictable for the following reasons: (1) the recombinant mutant allergen may increase IgE production and binding, (2) the recombinant mutant allergen may be inactivated before producing an effect, for instant, due to proteolytic degradation or immunological inactivation as a consequence of the inherently short half-life, this led to a lack of allergen specific antibody production; (3) other functional properties, known or unknown, may

make the recombinant mutant allergen unsuitable for in vivo therapeutic use, i.e. such as adverse side effects of unwanted immune suppression that prohibit the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In view of the quantity of experimentation necessary, the lack of in vivo working examples, the unpredictability of the art, the insufficient guidance with respect to the appropriate modifications within the full-length polypeptide of any allergen from any taxonomic order and the breadth of the claims, one skilled in the art could not use the claimed invention without undue amount of experimentation.

Applicants' arguments filed 6/10/02 and the declaration of T. P. King filed on 4/10/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) Dr. King confirms that at the time the invention was made, the specification provides sufficient support to enable one of ordinary skill in the art to make and use the claimed recombinant mutant allergens as vaccines against IgE-mediated allergic reactions, (2) the three references which demonstrate the state of the art with respect to (i) predicting the structural similarity or homologous proteins, (ii) constructing three-dimensional models of allergen protein structure, and (iii) identifying specific amino acid residues within B cell epitopes involved in antibody binding based on the three dimensional structures.

However, the specification discloses only two recombinant allergens from birch pollen major allergen comprising SEQ ID NO: 37 from the taxonomic order of *Fagales* and vaspid venom Ves v 5 comprising SEQ ID NO: 38-39 from the taxonomic order of Hymenoptera. Further, there are no in vivo working examples demonstrating that any recombinant allergens or any recombinant modified allergen from any taxonomic orders are effective in prevent all allergy. Skolnick *et al* teach that squence-based methods for function prediction are inadequate and knowing a protein's structure (amino acid sequence) does not necessary tell one it's function (See entire document, Abstract in particular). Attwood *et al* teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable (See figure, entire document). Branden et al (PTO 1449) teaches there are no methods available today to model a tertiary structure from the amino acid sequence alone and obtain a model detailed enough to be of any use, for example, in drug design and protein engineering (See page 350, in particular). Branden *et al* further teach secondary structure cannot in general be predicted with a high degree of confidence with the possible exceptions of transmembrane helices and α-

helical coiled coils (See page 350, in particular). Contrary to Dr. King's position that one of ordinary skill in the art could determine which amino acids and the specific type of amino acid within the full-length amino acid sequence of any recombinant allergen could be substituted, Lederman *et al* teach that even a single amino acid substitution can ablate the binding of the monoclonal antibody to the protein (See abstract, in particular). Abaza *et al* teach amino acid substitution even outside the protein antigenic sites can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the lack of guidance as to which specific amino acid within the B cell epitope of any allergen mentioned above can tolerate change, it is unpredictable which undisclosed recombinant mutant allergen would bind to the allergen specific antibody, in turn, would reduce the binding between the allergen and the IgE and be useful as a vaccine against any allergies.

9. Claims 2-14, 16-28, 32-34, 47-49 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* recombinant mutant allergen derived from *any* naturally occurring allergen in which at least one surface-exposed, *any* amino acid residue of a B cell epitope at *any* position which is conserved in *any* amino acid sequences of *any* homologous proteins within the taxonomic order from which the naturally occurring allergen originates, is substituted with *any* amino acid residue which is not conserved in the same position in the amino acid sequences of any homologous proteins within the taxonomic order from which the naturally occurring allergen originates, wherein the α-carbon backbone tertiary structure of *any* naturally occurring allergen, and specific IgE binding to *any* mutant allergen is reduced compared to the IgE binding to *any* naturally occurring allergen, (2) *any* recombinant allergen mentioned above obtainable by a) identifying *any* amino acid residues in *any* naturally occurring allergen which are conserved with more than 70% identity in all known homologous proteins within the taxonomic order from which said naturally occurring allergen originates, (b) defining at least one patch of conserved amino acid residues being coherently connected over at least 400 $Å^2$ of the surface of the thee-dimensional structure of *any* naturally occupying allergen molecule as defined by having a solvent accessibility of at least 20%, said at least one patch comprising at least one B cell epitope and (c) substituting at least *any* one amino

acid residue in said *any* one patch with another non-conservative amino acid, wherein the α-carbon backbone tertiary structure of the allergen molecule is conserved, (3) *any* recombinant allergen mentioned above wherein the specific IgE binding to the mutant allergen is reduced by at least 5%, preferably by at least 10%, (4) *any* recombinant allergen mentioned above wherein the average root mean square deviation of the atomic coordinates comparing the α-carbon backbone tertiary structures of *any* mutant and the naturally occurring allergen molecules is below 2 Å, (5) *any* recombinant allergen obtainable by the process of claim 2 wherein said at least *any* one patch consisting of *any* 15 amino acid residues, (6) *any* recombinant allergen obtainable by the process of claim 2 wherein the amino acid residues of *any* one patch are ranked with respect to solvent accessibility and *any* one or more amino acids among the more solvent accessible ones are substituted, (7) *any* recombinant allergen mentioned above wherein one or more amino acid residues of *any* one patch having a solvent accessibility of 20-80% are substituted, *any* 1-5 amino acids residues per 400 $Å^2$ in any one patch are substituted, *any* substitution of one or more amino acid residues in any B cell epitope or *any* one patch is carried out by site-directed mutagenesis, (8) *any* recombinant allergen mentioned above wherein the allergen is derived from *any* inhalation allergen, *any* pollen allergen, *any* pollen allergen originating from the taxonomic order of Fagales, Oleales or inales, (9) *any* recombinant allergen derived from Bet v1 wherein at least *any* one amino acid residues of said B cell epitope or said at least *any* one patch is substituted, (10) *any* recombinant allergen mentioned above derived from inhalation allergen wherein the allergen is a pollen allergen derived from *any* pollen allergen originating from the taxonomic order of Poales, Asterales, or Urticales, house dust mite, mite allergen from Dermatophagoides, cockroach allergen, *any* animal allergen such as the ones from cat, dog or horse, venom allergen originating from the taxonomic order of Hymenoptera, Vespidae, Apidae and Formicoidae, *any* allergen derived from Ves v5 (11) *any* recombinant allergen wherein the allergen is derived from any venom allergen wherein at least one amino acid is substituted such as the substitution is from Lys to Ala at position 72 or from Tyr to Ala at position 96, (12) *any* recombinant allergen mentioned above for use as a pharmaceutical, (13) *any* pharmaceutical composition comprising *any* recombinant allergen mentioned above optionally in combination with *any* pharmaceutical acceptable carrier and/or excipient, and optionally an adjuvant, (14) *any* pharmaceutical composition mentioned above in the form of a vaccine against allergic reactions elicited by any naturally occurring allergen in patients suffering from allergy, (15) *any* pharmaceutical composition obtainable by the process such as the process recited in claim 48, and (16) *any*

recombinant allergen obtainable by the process recited in claim 2 wherein said at least one patch consists of at least *any* 15 amino acid residues, or *any* 15-25 amino acid residues for a vaccine.

The specification discloses only two recombinant allergens from birch pollen major allergen comprising SEQ ID NO: 37 from the taxonomic order of *Fagales* and vaspid venom Ves v 5 comprising SEQ ID NO: 38-39 from the taxonomic order of Hymenoptera. The specification discloses recombinant mutant allergen from birch pollen major allergen comprising SEQ ID NO: 37 wherein said allergen has one or more amino acid substitutions such as the ones disclosed on page 27 lines 25-32 of the specification or the ones recited in claim 50. The specification further discloses recombinant mutant allergen from vaspid venom Ves v 5 comprising SEQ ID NO: 38-39 having one or more amino acid substitutions such as the ones disclosed on page 44-46. The said recombinant mutant allergens obtainable by the method recited in claim 2 for treating allergic reactions.

With the exception of the specific recombinant mutant allergens mentioned above, there is insufficient written description about the structure associated with functions of (1) *any* recombinant allergen ...substituting *any* amino acid residue of any B cell epitope at *any* position, (2) *any* allergen is derived from any pollen allergen, (3) *any* amino acid residue of B epitope or (4) *any* one patch is substituted, (5) *any* recombinant allergen derived from Poales, Asterales or Urticales, house dust mite allergen, mite allergen from Dermatophagoides, cockroach allergen, any allergen derived from any animal allergen, any animal allergen originating from cat, dog or horse, venom allergen, venom allergen originating from the taxonomic order of Hymenoptera, Vespidae, Apidae and Formicoide, or from Ves v5, (6) *any* pharmaceutical composition comprising *any* recombinant allergen, (7) *any* recombinant mutant allergen derived from *any* naturally occurring allergen for a pharmaceutical composition in the form of a vaccine against allergic reactions. Further, Applicant discloses only two recombinant mutant allergens; there is a lack of a written description of *any* additional representative species of recombinant allergen, or recombinant mutant allergen for a vaccine composition, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. Claim 50 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
August 26, 2002

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